H_T30Q and L_Y49W and L_Y96G; or

H_T30Q and H_G56Y and L_Y49W.

86. The antigen-binding construct of claim **80**, wherein the Glycine at position 56 of CDR-H2 has been substituted with a Tyrosine (H_G56Y) and the Serine at position 99 of CDR-H3 has been substituted with a Tryptophan (H_S99W), numbering according to Kabat numbering system.

87. The antigen-binding construct of claim **80**, wherein the variant first antigen-binding polypeptide construct is a Fab.

88. The antigen binding construct of claim **87**, further comprising a first linker polypeptide operably linked to the variant first antigen-binding polypeptide construct.

89. The antigen-binding construct of claim **88**, wherein the first linker polypeptide is operably linked to a heterodimeric human IgG1 Fc comprising a first Fc polypeptide and a second Fc polypeptide each comprising a different CH3 sequence.

90. The antigen-binding construct of claim **80**, wherein the antigen-binding construct comprises a second antigen-binding polypeptide construct that binds to a second antigen.

91. The antigen-binding construct of claim **90**, further comprising a first linker polypeptide operably linked to the variant first antigen-binding polypeptide construct, and a second linker polypeptide operably linked to the second antigen-binding polypeptide construct.

92. The antigen-binding construct of claim **90**, wherein the second antigen is a HER2 ECD2 antigen and the second antigen-binding polypeptide construct is identical to the variant first antigen-binding polypeptide construct.

93. The antigen-binding construct of claim **90**, wherein the second antigen is a HER2 ECD4 antigen and the second antigen-binding polypeptide construct is an scFv comprising the VH and VL domain of trastuzumab and a glycine-serine linker.

94. The antigen-binding construct according to claim **91**, wherein the first and second linker polypeptides are operably linked to a heterodimeric human IgG1 Fc comprising a first Fc polypeptide and a second Fc polypeptide each comprising a different CH3 sequence.

95. The antigen-binding construct of claim **94**, wherein the CH3 sequence of each Fc polypeptide comprises one or more modifications that promote the formation of a heterodimeric Fc with stability comparable to a wild-type homodimeric Fc, the heterodimeric IgG1 Fc having

a) the modifications L351Y_F405A_Y407V in the first Fc polypeptide, and the modifications T366L_K392M_T394W in the second polypeptide; or

b) the modifications L351Y_F405A_Y407V in the first Fc polypeptide, and the modifications T366L_K392L_T394W in the second Fc polypeptide; or

c) the modifications T350V_L351Y_F405A_Y407V in the first Fc polypeptide, and the modifications T350V_T366L_K392L_T394W in the second Fc polypeptide; or

d) the modifications T350V_L351Y_F405A_Y407V in the first Fc polypeptide, and the modifications T350V_T366L_K392M_T394W in the second Fc polypeptide; or

e) the modifications T350V_L351Y_S400E_F405A_Y407V in the first Fc polypeptide, and the modifications T350V_T366L_N390R_K392M_T394W in the second Fc polypeptide; or

f) the modifications T350V_L351Y_F405A_Y407V in the first Fc polypeptide, and the modifications T366I_N390R_K392M_T394W in the second Fc polypeptide; or

g) the modifications L351Y_S400E_F405A_Y407V in the first Fc polypeptide, and the modifications T350V_T366L_K392L_T394W in the second Fc polypeptide,

wherein the numbering of amino acid residues in the Fc is according to the EU numbering system.

96. A pharmaceutical composition comprising the antigen-binding construct of claim **80**, and a pharmaceutical carrier, optionally selected from a buffer, an antioxidant, a low molecular weight molecule, a drug, a protein, an amino acid, a carbohydrate, a lipid, a chelating agent, a stabilizer, or an excipient.

97. An isolated polynucleotide or set of isolated polynucleotides comprising at least one nucleic acid sequence that encodes the antigen-binding construct of claim **80**, optionally wherein said polynucleotide or set of polynucleotides is cDNA.

98. An isolated cell comprising a polynucleotide or set of polynucleotides according to claim **97**, the isolated cell optionally selected from a hybridoma, a Chinese Hamster Ovary (CHO) cell, or a HEK293 cell.

99. A method of treating a subject having a HER2-expressing (HER2+) cancer, optionally wherein the cancer is breast cancer or gastric cancer, the method comprising administering to the subject the antigen-binding construct of claim **80**.

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